

Supporting Information for

Inactivation Switch for Run-up in TRPV2

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This supplementary material includes:

Table S1: Tertiary noncovalent interactions in 2-APB-activated rTRPV2 at 4 °C (PDB ID: 7N0N).

Table S2: Tertiary noncovalent interactions in 2-APB-inactivated rTRPV2 at 4 °C (PDB ID: 7N0M).

Table S3: Tertiary noncovalent interactions in DMNG-inactivated rTRPV2 at 4 °C (PDB ID: 5HI9).

Table S4: Tertiary noncovalent interactions in 2-APB/PBC-activated rTRPV2 at 4 °C (PDB ID: 9B3V).

Table S1. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of 2-APB-activated rTRPV2 in DMNG/MSP2N2 at pH8 and 4 °C (PDB ID, 7N0N).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	R328-D344, D349-R684, E358-R459-E670, R369-D469, R388-E685, K531-E647
H-bond	<3.9 Å donor-H-acceptor <60°	V254/M255-K307, D258-S260, Y271-E288-R317, N292-L296, Q294-K304, T297- K300-N354 , K304-C364, G306-N368, Q316-Y343, E318-Q324, S327-R702, R328-S346, K329-Y343, E332-R706, D344-S346-S347, S350-E672, S355-E358, S366-N368, H370-S658, K385-L381, Y403-Q479, Q452-E473, R458-E670, S466-S470, S486/R490-Y497, Y514-S667, I524-S656, S526-Q530, Y544-T604-L600, Y544-Y629, S559-P589, E672-R680, N673-R679
π - π interaction ²⁶	2.65–6.5 Å	W333-Y335, F362-F462, W386-F393-Y515, F394-F397, F394/F397-F519, F397-Y515, Y400-Y403-Y407, Y400-F476, Y400-Y515, Y412-H413, H438-F491, Y447-Y675/W676, W454-W676, Y455-F456, Y471-F472-Y514, F476-Y514/Y515, Y514-Y515, Y544-F601, F551-Y629, W657-W660, W676-W677, W712-W715
cation- π interaction	<6.0 Å	W351-R684-W703, F362-R459, W386-K664, R388-H683, W457-R460, R684-W703
CH ₃ /CH- π interaction	2.65-3.01 Å	I268-H313, Q276-Y323, F330-V691, W333-V340, Y343-P377, P337-W712/W715, L381-F705, F405-V409, I463-W464, Y497-L498, F540-M640, L600-Y629-T633, R617-F618, W657-K661, W660-K664, L688-W703, W715-L719
Lone pair- π interaction	3-3.7 Å	Q276-F319, F311-M372, F429-S432, Y455-E473

Table S2. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of 2-APB-inactivated rTRPV2 in DMNG/MSP2N2 at pH8 and 4 °C (PDB ID, 7N0M).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	E288-R317, E309-R312, E332-R687, D349-R684, R369-D469, K385-E685, E561-R617, R706-E708
H-bond	<3.9 Å donor-H-acceptor <60°	M255-K307, D258-N263, N259-N368, Y271-E288, D272-H313, R280-Y323, N292-L296, A303/K304-C364, G306-N368, Q316-E376, R317-L326/S327/R328/K329, P325/S327-R702, R328-S346, T331-L722, E332-S723-T721, D344-S346/R702, N368-R371, H370-S658, N396-Y675, Y400-G508, T408-W509, Q414-H438, Y447-W677, Q452-E473, S466-D469, M468-Q530, Q479-S504, L475-N511, Q487-R490, Y544-T604/Y629, R563-Q615, S592-D595, L600-Y629, H651-S656, G692-D700
π - π interaction	2.65–6.5 Å	F362-F462, W386-F393-Y515, F394-F519, F397-Y515, Y400-Y403, Y400-F476, Y400-Y515, Y412-H413, Y447-W676, W454-W457/W676, Y455-F456, F467-Y471, F472-F476, F472-Y514, F476-Y514/Y515, Y514-Y515, F540-Y544-F601, F551-Y629, F603-Y629, W657-W660, W676-W677, W712-W715
cation- π interaction	<6.0 Å	F362-R459, R392-Y675, H438-R490, W454-R458, W457-R460, R684-W703
CH ₃ /CH- π interaction	2.65-3.01 Å	I268-H313, Q276-Y323, K329-Y343, F330-V691, W333-P726, P337-W712, W351-R684, L381-F705, W386-K664, R490-Y497, V543-F547, Y544-L548, F549-V553, L555-Y590, R617-F618, W657-K661, L688-W703
Lone pair- π interaction	3-3.7 Å	Q276-F319, F476-N511, Y629-T633, W677-C678

Table S3. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of PE-free inactivated rTRPV2 in DMNG at pH 8 and 4 °C (PDB ID, 5HI9).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	D536-R539-E647, E561-R617, E614-R619
H-bond	<3.9 Å donor-H-acceptor <60°	M255/A257-K307, D258-N263, S260-E262, Y271-E288, D272-H313, E288-R317, N292-L296, I314-R317-T331, E332-R694/C704, D344-C704, S347-N354/S355, D349-K385, D349/S350-S355, H363-K365, N374-N379, K385-R687, T408-W509, Y447-R679, Q452-E473, S466-S470, M468-K531, G444-Q479-T483, L482-S504, Q487-R490, T516-S526, R517-W660, Y544-T604, E599-K602, K602-E609, R684-R687, R694-D700, E709-N711
π - π interaction	2.65–6.5 Å	W351-W703, F362-Y455, H363-F462, W386-F393-Y515, F394-F519, F397-Y515, Y400-F476, F405-W509, Y412-H413, Y447-W677, W454-W676/W677, Y455-F456, F467-Y471, Y471-F472-Y514, F476-Y514/Y515, Y514-Y515, H521-Y525, F551-Y629, Y675-W677
cation- π interaction	<6.0 Å	Y514-R517, W657-K661, W660-K664
CH ₃ /CH- π interaction	2.65-3.01 Å	I268-H313, W351-E685, F362-L669, W386-V390, W386-K664, M404-W509, H521-W660, V546-F549, L688-W703
Lone pair- π interaction	3-3.7 Å	W351-E352

Table S4. Tertiary noncovalent interactions along the PE-dependent minimal gating pathway from V254 to P726 in each subunit of 2-APB-PBC-activated state 2 of rTRPV2 in DMNG/MSP2N2 at pH 8 and 4 °C (PDB ID: 9B3V).

Noncovalent interaction	Cut-off distance	Linked residues
Salt bridge	3.2-4 Å	D344-R702, E599-K602,
H-bond	<3.9 Å donor-H-acceptor <60°	V254/M255/A257-K307, S291-G295, N292-Q294-K304, N292-L296, K300-N354 , A303/K304-C364, G306-N368, R317-L326/R328/K329, F319-S327, G321-Q324-S327, Y323-S327, P325/S327-R702, R328-D344, T331-C334, R339-E709, S341-Y343, D344-S346, D349-K385, I360/A361-R369, S366-N368, Q383-K661, K385-E672, Y403-Q479-T483, V410-Q414-H438/Y497, L434-H438, Q452-E473, S486-Y497, Y514-S667, T516-T522, R517-W660, D536-R539, Y544-T604/Y629, E561-R617, L600-Y629, Q613-Q615, H651-A652, Y675-R679, R706-E708, N711-A714, W715-T718
π - π interaction	2.65–6.5 Å	W351-W703, W386-F393-Y515, F393-F394, F394/F397-F519, F397-Y515, Y400-Y403-F407, Y400-F476, Y400-Y515, Y412-H413, Y447-W676/W677, W454-W457/W676, Y455-F456, Y471-F472-Y514, F476-Y514, Y514-Y515, Y544-F601, F547-F551, F551-Y629, F603-Y629, W657-W660, W676-W677-Y675, W712-W715
cation- π interaction	<6.0 Å	W386-K664, F362-R459, H438-R490
CH ₃ /CH- π interaction	2.65-3.01 Å	I268-H313, Y271-I314, F311-L315, F330-V691, W333-V340, P337-W712/W715, Y343-P377, W351-R684, A361-F362, W386-V390, M404-W509, F405-V409, F407-I441/L505, V410-H438, Y455-R459, F519-H521, F540-Y544/M640, V543-F547, F612-R619, R617-F618, V630-Y634, W657-K661, W660-K664, R684/L688-W703
Lone pair- π interaction	3-3.7 Å	H370-N655, Y455-E473, F476-N511, F476-PE-Y515, F601-T604, Y629-T633